

I

A NEW METHOD FOR THE MANAGEMENT OF GONORRHŒA *

By P. A. CLEMENTS, M.B., B.S. ; Senior Medical Officer,
Venereal Department, St. Thomas's Hospital.

(Director, Colonel L. H. Harrison).

FROM the advertised title of this paper, you may be expecting to hear something completely new, and perhaps will be disappointed to find that there is much that you have heard before. Admittedly the treatment of gonorrhœa is difficult, but one is inclined to think that in the past too much attention has been paid to treatment in the form of local applications of antiseptics and drugs in their many forms. For example, I believe there are some forty odd preparations of silver on the market, most of which have been advocated for the treatment of this disease, and in spite of them all it is generally admitted that the cure of gonorrhœa is a very uncertain business.

Some time in 1915, when I first became associated with the management of venereal diseases, I remember Colonel Harrison expressing the belief that the cure of gonorrhœa would eventually come through the blood. Since that time numerous antiseptics have been discovered, and the reaction to the publication of most of them has been a trial of them in gonorrhœa. It seems as if everyone had a pathetic belief that sooner or later the gonococcus could be bludgeoned out of its dug-outs by a frontal attack. Although many such antiseptics have been reported on favourably at first, none has survived and been universally accepted as an advance on older local remedies.

I can never understand why gonorrhœa should be the one disease singled out of the whole of medicine to be treated in this manner. One does not attempt to combat other acute infections in this manner ; why gonorrhœa ?

As an example of what I regard the futility of merely local treatment, and one which I have seen frequently carried out, is the application of remedies to a cervical

* Based on an address delivered before the M.S.S.V.D., April 28th, 1933.

BRITISH JOURNAL OF VENEREAL DISEASES

erosion. Surely the disease is limited to the cervix in only a small percentage of cases of female gonorrhœa. Additionally, it is conceivable that prolonged local applications are definitely harmful, and may tend to prolong an attack of gonorrhœa in that they interfere with local immunity and the production of antibodies. One can recall persistent cases treated for prolonged periods by local applications which, on suspension of this form of treatment, have cleared up and cured themselves.

During the past two years we have been working on the principle that, the main infection being submucous, local applications play only a minor part in the cure of gonorrhœa. We believe, in fact, and think our results show, that the recovery of a patient from gonorrhœa depends on two factors:—

- (1) Resistance to the gonococcus ;
- (2) Efficient drainage.

Without these no local remedy avails. Accordingly, our local treatment has consisted of daily cleansing, urethral irrigations in the male, and in the female urethral and cervical irrigations with some mild antiseptic lotion, and often tampons soaked in glycerine with some antiseptic in weak concentration. I am not at all sure whether this is too much in the female, and I am inclined to think that in acute cases the cervix is perhaps better not irrigated, but the patient given hot vaginal douches ; these, of course, being given in the department, and not entrusted to the patient herself. Our local treatment has, in fact, been designed to avoid any interference with natural drainage, but rather to assist this as much as possible. In later stages we have kept continually before us the possibility of badly draining foci being present, and frequently have found that discovery and treatment of such foci have brought a resistant case to a happy termination.

Drainage may, however, be perfect, but the disease persists. In such cases we have found the cause to be in defective resistance as judged by the complement fixation test. Our problem has then been to raise the resistance, and in this we have found the use of the vaccine, which will be described by Dr. Oliver, particularly good.

With regard to the measurement of the resistance by the complement fixation test, we have found that in a

MANAGEMENT OF GONORRHOEA

large proportion of the cases in which gonococci can be isolated after months of local treatment, and in cases in which the disease is supposed to have been present for prolonged periods before seeking advice, the complement fixation reaction has remained negative or doubtful, and often also in these cases the clinical signs have been slight, as if the tissues were tolerating the infection without great protest. Coincidentally with a rise in the titre of the complement fixation reaction, effected by carefully regulated administration of vaccine, the gonococci have usually disappeared. Conversely, in a number of cases in which the complement fixation has not been increased in strength by these means, the gonococci have remained.

In the very great majority of our cases in which gonococci have persisted in spite of a high complement fixation titre, we have found the drainage at fault, and, on remedying this, the disease has been eradicated.

With regard to the details of the management of gonorrhœa, I will confine myself to those relating to the measurement and artificial raising of the resistance. The blood for the complement fixation reaction should be taken as far as possible at the same interval of time after the last dose of vaccine, as we have found the strength of this to vary considerably from day to day, especially in those cases in which the reaction is not very strong. At this point I should like to acknowledge the valuable assistance we have received from Dr. Hughes, who has carried out all the serum tests connected with this investigation.

The vaccine I have used chiefly for the past two years, and which we have termed "ecto-antigen," has been prepared by Dr. Oliver, of St. Thomas's Hospital, on the principle elaborated by Dimond at the Royal Herbert Hospital, Woolwich, some years ago.

It is injected intra-cutaneously in the region of the groins, the idea being to give the vaccine as near to the site of infection as convenient; also the skin in that area appears to lend itself very suitably for intra-cutaneous injections. The dosage has to be watched very carefully, as patients respond in respect of local, focal, and general reactions very differently. The local reaction may vary from a slight erythema to a large angry patch 5 inches or 6 inches in diameter. In complicated cases there is frequently well-marked focal reaction, as for instance in the

BRITISH JOURNAL OF VENEREAL DISEASES

case of an acute joint, one usually finds an increase in the amount of the fluid present within two to three hours, which continues to increase up to forty-eight hours or so, and then gradually subsides. This is contrary to the result one gets when using shock therapy, and disposes of the suggestion that might be brought forward that our results may be due to this and not to a specific effect of the vaccine.

As for the general reaction, this varies from a mild rise of temperature to a severe rigor with fever to 104° . I have seen 0.1 c.c. of the vaccine produce a rigor in one person, and a dose of 1.5 c.c. out of the same bottle cause very little apparent ill-effect of any kind in another.

During the early days, before we had much experience, our dosage was perhaps a little too heroic, and I fear that in consequence some of our patients developed rather alarming complications.

Those who are interested in the management of venereal diseases more from a public health point of view might argue that these reactions which sometimes occur would tend to frighten patients into defaulting from the treatment centre. In practice we have found this to be to the contrary, as the percentage of cases defaulting after commencing treatment with ecto-antigen is a fraction over 10 per cent., as compared with approximately 30 per cent. for other cases of gonorrhœa attending the clinic during the year 1932.

This I attribute to the fact that the patients imagine that they are receiving more personal interest and attention, and are willing to undergo considerable discomfort in their efforts to rid themselves of their infection.

Regarding the actual administration of the vaccine, a safeguard must be taken of not injecting any into a small vein, which, I believe, although it has not happened to me, results in very extensive thrombosis. As a point of interest, the person who does not react in any way, and can stand large doses of the vaccine, with little local or no general discomfort, appears to make only moderate progress both clinically and bacteriologically. We have not found it practicable to carry out the remainder of the procedure prescribed by Dimond, such as bringing the pH of the urine to a given titre.

I think the vaccine is more successful in raising the

MANAGEMENT OF GONORRHŒA

titre of the complement fixation reaction than are ordinary gonococcal vaccines. In a number of our cases we have found the complement fixation reaction negative, even after prolonged courses of ordinary vaccines ; shortly after instituting treatment with ecto-antigen, the titre of the complement fixation reaction has risen to a high point, and the gonococci have disappeared. It is true that the route of administration, the intra-cutaneous as opposed to the sub-cutaneous, might account to some extent for the difference in the results. On this point I have only a little evidence, but so far as this goes, it indicates that the ecto-antigen we have used affords better results than does ordinary gonococcal vaccine administered intra-cutaneously.

To summarise : my observations, which have been made in collaboration with Dr. Oliver, have convinced me that, in the absence of a chemo-therapeutic agent which will destroy the gonococcus through the blood stream, the best hope of curing gonorrhœa lies in efficient drainage, and in raising the resistance to the highest possible level, and that the best means of raising the resistance is by the use of a properly chosen vaccine correctly administered ; also that the complement fixation reaction is a good indication of the success or otherwise of efforts in this direction.

I have attempted to illustrate by means of graphs, prepared from the case cards of patients, some of the points which I have mentioned. Before I show these, I should like to state that I do not wish to leave the impression that our results are always good, but that they are sufficiently encouraging to denote that we are working on the right lines.

The graphs illustrate a few points from the clinical records of cases treated by ecto-antigen.

The vertical line represents the varying strength of the complement fixation reaction. The reactions up to and including ++ are the results of tests with undiluted serum, whilst in the remainder the serum has been diluted 5, 10, 20, 40, 80 times with saline.

The horizontal line represents the period of time over which the cases were observed.

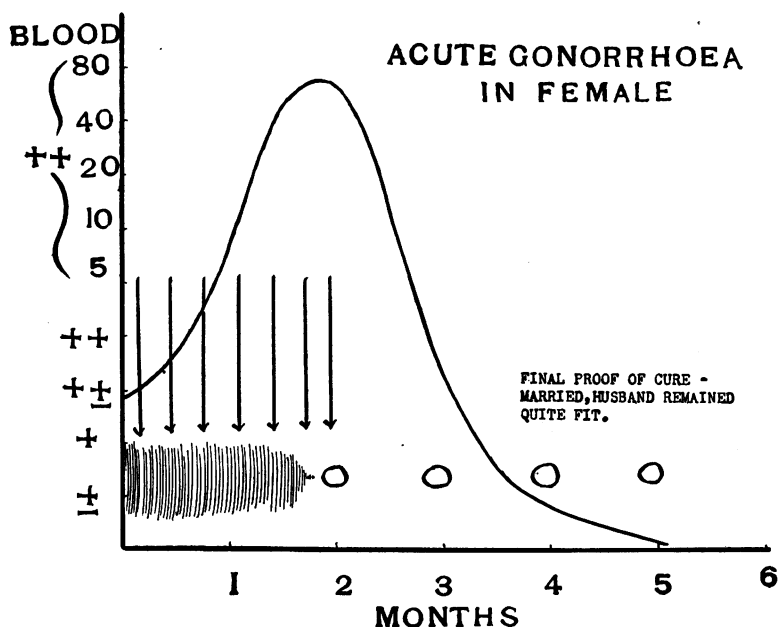
The vertical shaded lines represent the period over which gonococci were found either in culture or smear, or both.

BRITISH JOURNAL OF VENEREAL DISEASES

The vertical arrows represent the period over which the patient was treated with ecto-antigen.

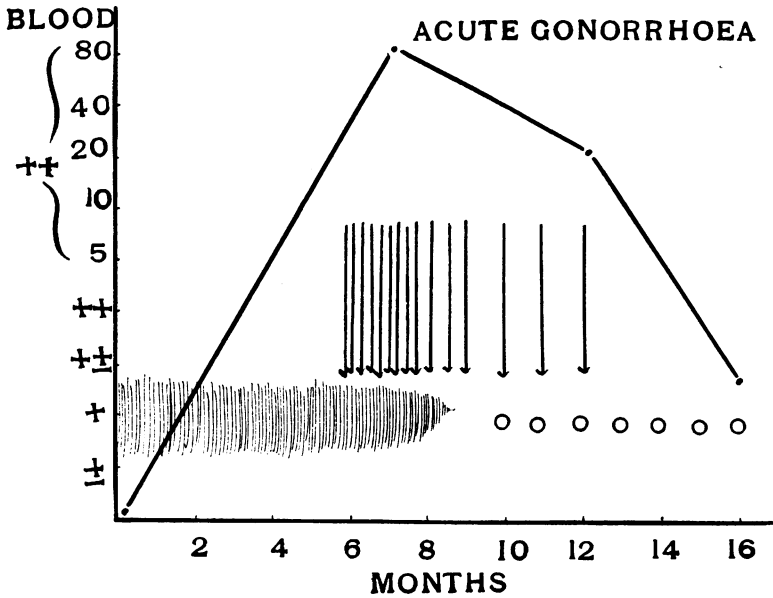
The circles denote negative tests in which there was no clinical evidence of active gonococcal infection and failure to identify the gonococcus in either smear or culture.

The curves illustrate the varying strength of the complement fixation reaction before, during, and after treatment with ecto-antigen ; whilst in two of the cases an extra curve represents the state of the joints during the progress of the case.

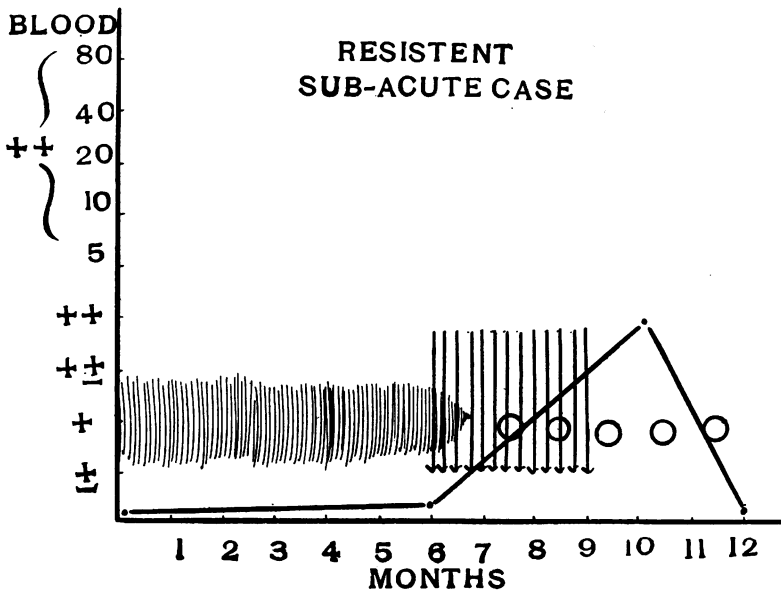


1.—Acute Gonorrhœa in Female. Increase strength of Complement Fixation Reaction by Ecto-antigen ; Disappearance of Gonococci, and eventual cure of patient ; Rapid fall in strength of Complement Fixation Test.

MANAGEMENT OF GONORRHŒA

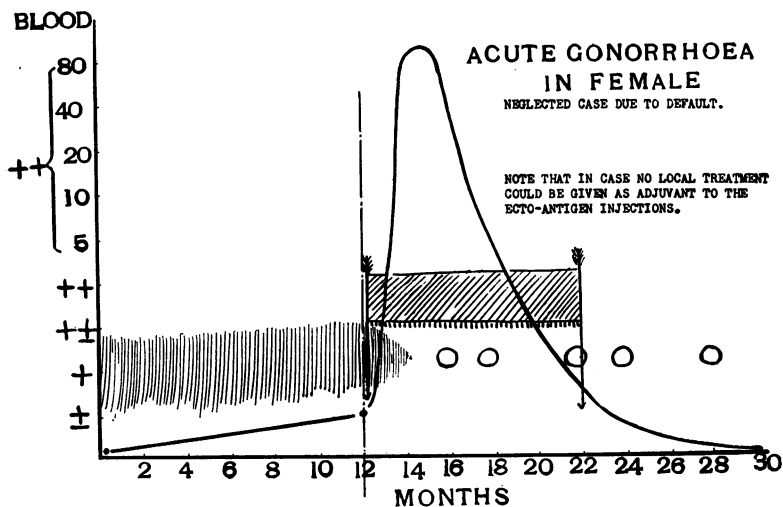


- 2.—Acute Gonorrhœa. Patient tending to make her own resistance, but still has difficulty in eliminating Gonococci. Titre of Complement Fixation Reaction increased with Ecto-antigen, and Gonococci disappear.

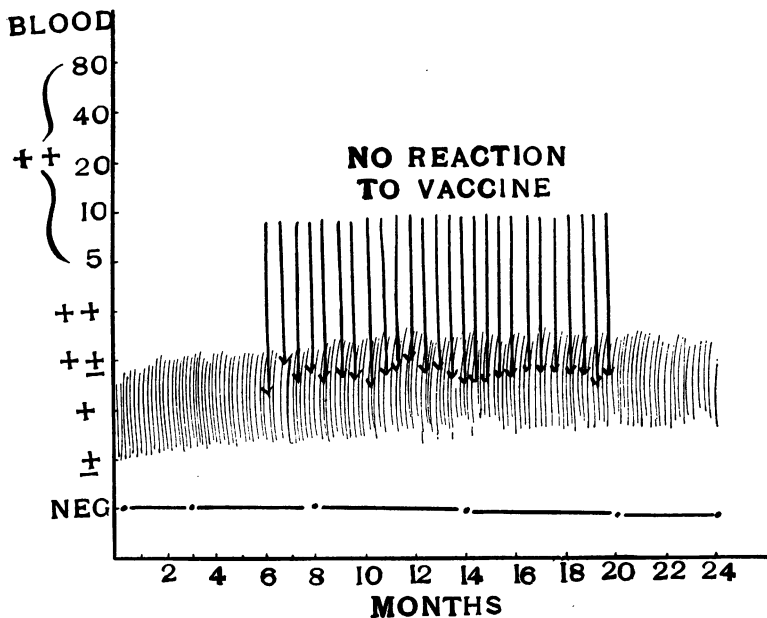


- 3.—Sub-acute Gonorrhœa. Gonococci present for over six months. Practically no increase in Complement Fixation Reaction. Titre of Complement Fixation Reaction increased with Ecto-antigen, and Gonococci disappear.

BRITISH JOURNAL OF VENEREAL DISEASES

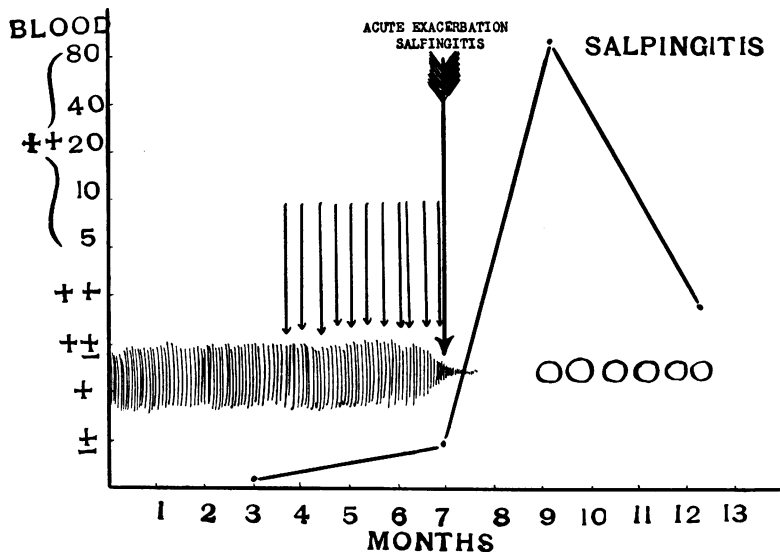


- 4.—Gonococci present for one year. Complement Fixation Reaction remains negative. Very strong reaction on commencing treatment with Ecto-antigen. Case clears up. No local treatment given whilst on Ecto-antigen.

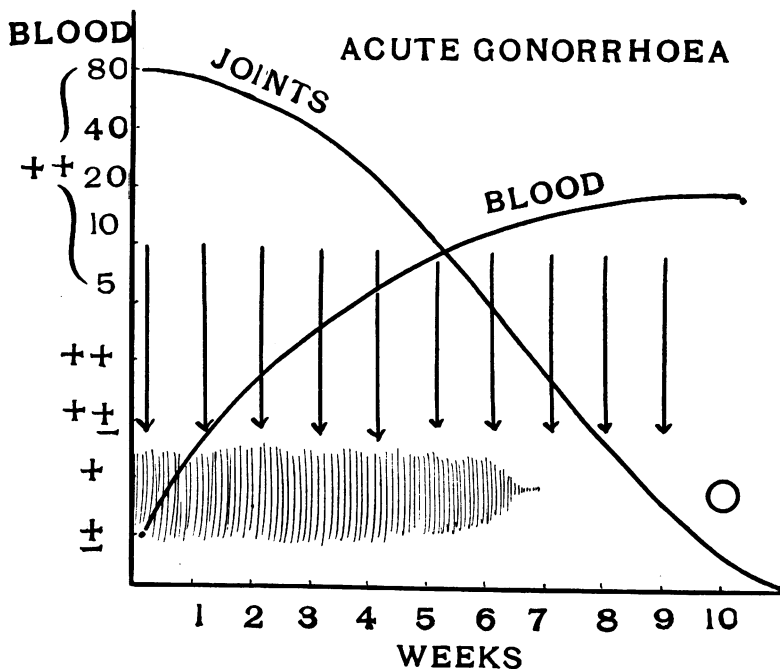


- 5.—Gonococci for six months. Complement Fixation Reaction remains negative. Ecto-antigen unable to increase resistance. Gonococci remain.

MANAGEMENT OF GONORRHOEA

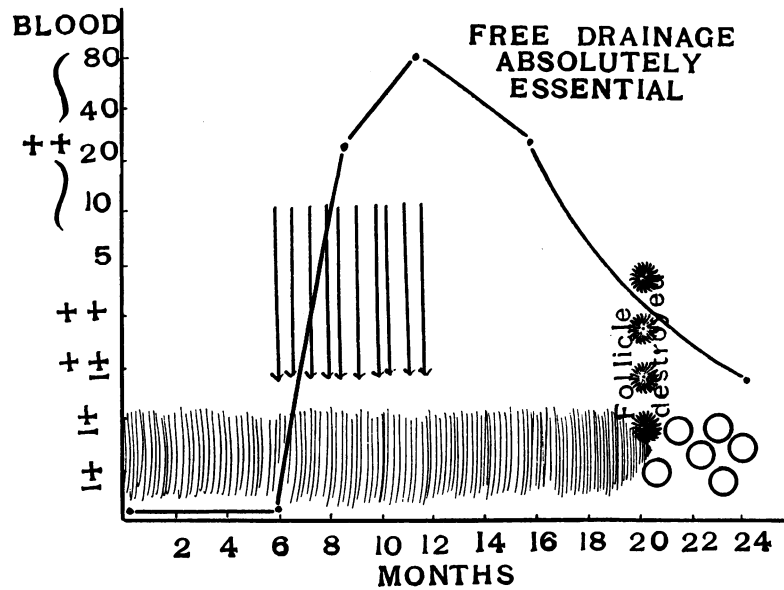


6.—Gonococci for three months. No change in Complement Fixation Reaction. Response to Ecto-antigen not great to begin with. Acute exacerbation. Salpingitis due to either (1) wrong dosage, or (2) enough resistance created to do battle with a quiescent tubal infection. Complement Fixation Reaction shoots up and patient cured.

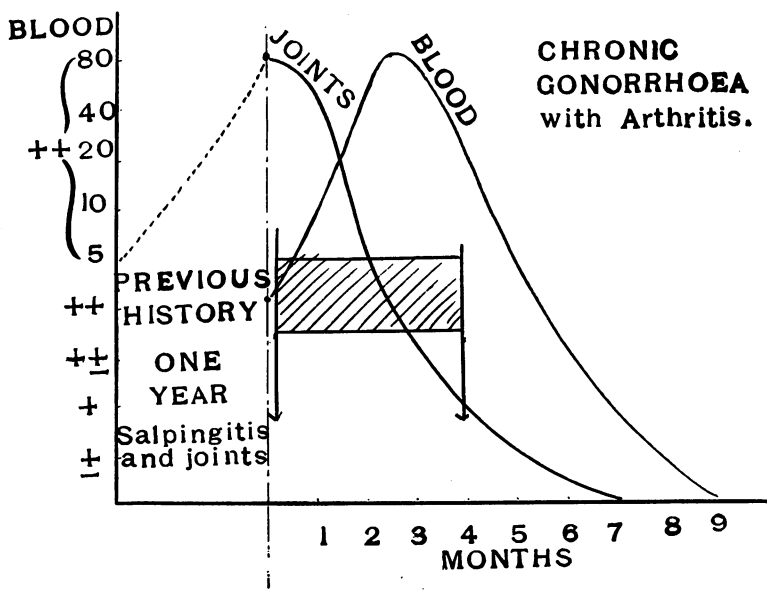


7.—Top curve represents condition of joints. As Complement Fixation Reaction goes up, joints rapidly improve.

BRITISH JOURNAL OF VENEREAL DISEASES

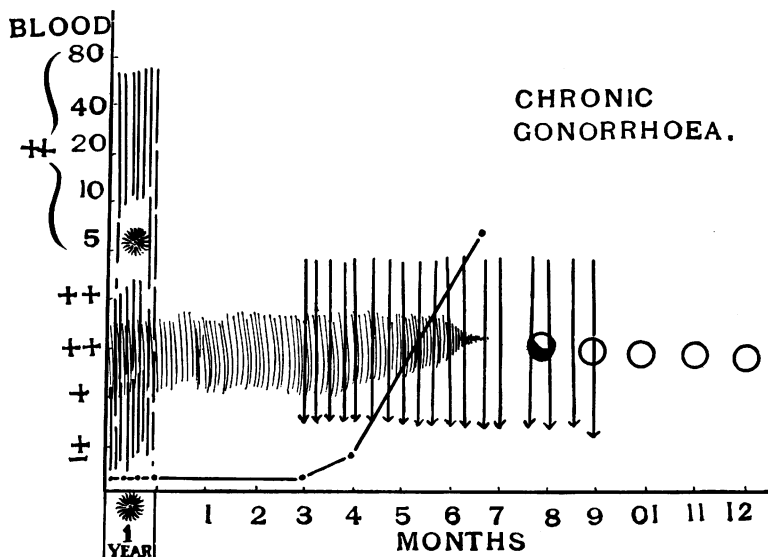


8.—Demonstrates drainage essential. Gonococci present for twenty months. Complement Fixation Reaction negative for six months. Complement Fixation Reaction pushed up, but no improvement until destruction of follicles, *i.e.*, badly draining foci.

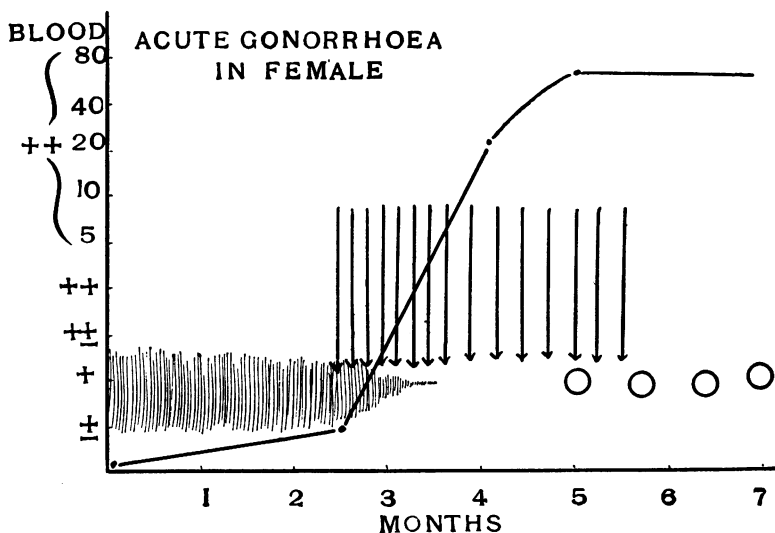


9.—History of Gonorrhoea with Salpingitis and Arthritis for one year. Treated privately. Complement Fixation Reaction not very strong. Ecto-antigen pushes reaction up, and joints, as represented by top curve, immediately improve.

MANAGEMENT OF GONORRHOEA

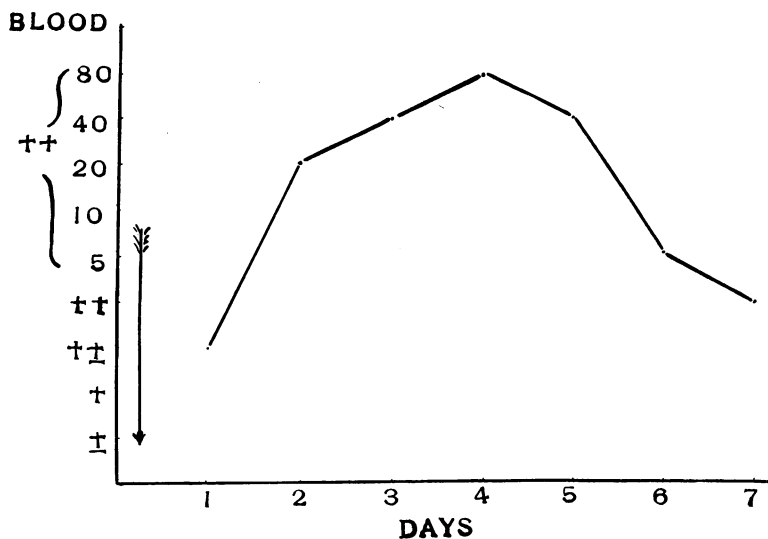


10.—Chronic Gonorrhœa for one year. Treated privately. Complement Fixation Reaction remains negative. Gonococci present. Complement Fixation Reaction increased only slowly, but patient eventually cured.



11.—Acute Gonorrhœa in Female. Gonococci present for ten weeks. Complement Fixation Reaction negative. Titre of Complement Fixation Reaction increased, and disease eradicated.

BRITISH JOURNAL OF VENEREAL DISEASES



12.—Daily variation of strength of Complement Fixation Reaction after an injection of Ecto-antigen demonstrates necessity of taking blood at same interval after injection in order to get a true idea of success in strengthening Complement Fixation Reaction.